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(19) (CA) **APPLICATION FOR CANADIAN PATENT** (12)

(54) Methods for Inhibiting Uterine Fibrosis

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(30) (US) 08/145,016 1993/10/28

(57) 9 Claims

5,097,6/89

Notice: This application is as filed and may therefore contain an incomplete specification.



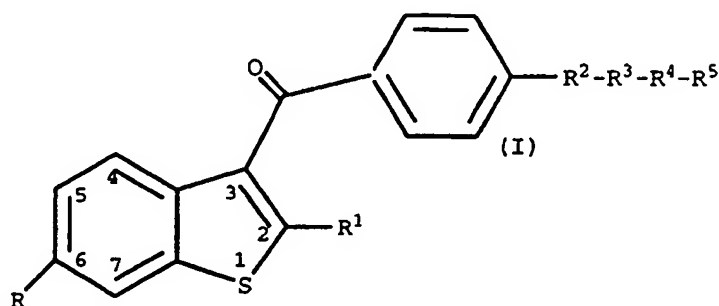
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ABSTRACT

A method of inhibiting uterine fibrosis comprising administering to a human in need of treatment an effective amount of a compound having the formula



wherein R is hydrogen; hydroxy; C<sub>1</sub>-C<sub>6</sub> alkoxy; a group of the formula -O-C(O)-R<sup>a</sup>, wherein R<sup>a</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with amino, halo, carbonyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, carbamoyl and/or aryl; or R<sup>a</sup> is C<sub>1</sub>-C<sub>6</sub> alkenyl optionally substituted with aryl; or R<sup>a</sup> is a C<sub>3</sub>-C<sub>7</sub> cycloalkyl; or R<sup>a</sup> is aryl optionally substituted with hydroxy, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, and/or halo; or R<sup>a</sup> is -O-aryl, said aryl optionally substituted with hydroxy C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, and/or halo,

or R is a group of the formula -O-SO<sub>2</sub>-R<sup>b</sup> wherein R<sup>b</sup> may be C<sub>1</sub>-C<sub>6</sub> alkyl or aryl optionally substituted with C<sub>1</sub>-C<sub>6</sub> alkyl;

or R is carbamoyloxy wherein the nitrogen may be substituted once or twice with C<sub>1</sub>-C<sub>6</sub> alkyl;

or R is a group of the formula -O-C(O)R<sup>c</sup>-O-(C<sub>1</sub>-C<sub>6</sub> alkyl) wherein R<sup>c</sup> is a bond or C<sub>1</sub>-C<sub>6</sub> alkanediyl;

R<sup>1</sup> is halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>7</sub> alkyl substituted with C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, or substituted or unsubstituted C<sub>3</sub>-C<sub>7</sub> cycloalkenyl;

R<sup>2</sup> is O or CH<sub>2</sub>;

R<sup>3</sup> is CH<sub>2</sub> or (CH<sub>2</sub>)<sub>2</sub>;

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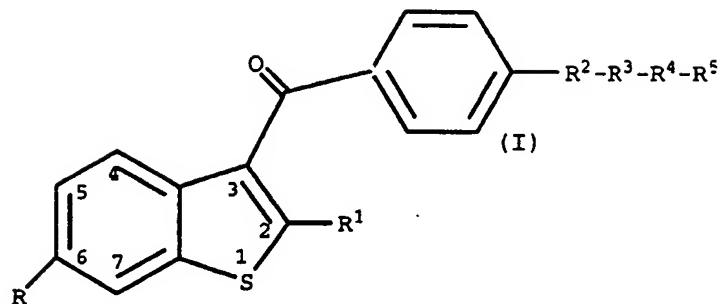
R<sup>4</sup> is  $\overset{\text{O}}{\parallel}\text{-C-}$ , CH<sub>2</sub>, or a bond; and

R<sup>5</sup> is amino, nitrilo optionally substituted once or twice with C<sub>1</sub>-C<sub>6</sub> alkyl; or an N-heterocyclic ring which optionally has another hetero atom selected from N, O, or S in said ring; or a pharmaceutically acceptable salt or solvate thereof.

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We claim:

1. A compound having the formula



wherein R is hydrogen; hydroxy; C<sub>1</sub>-C<sub>6</sub> alkoxy;  
 a group of the formula -O-C(O)-R<sup>a</sup>, wherein R<sup>a</sup> is  
 10 hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with amino,  
 halo, carbonyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, carbonyl, C<sub>1</sub>-C<sub>7</sub> alkanoyloxy,  
 carbamoyl and/or aryl; or R<sup>a</sup> is C<sub>1</sub>-C<sub>6</sub> alkenyl optionally  
 substituted with aryl; or R<sup>a</sup> is a C<sub>3</sub>-C<sub>7</sub> cycloalkyl; or R<sup>a</sup>  
 is aryl optionally substituted with hydroxy, C<sub>1</sub>-C<sub>6</sub>  
 15 alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, and/or halo; or R<sup>a</sup> is -O-aryl, said  
 aryl optionally substituted with hydroxy C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-  
 C<sub>6</sub> alkoxy, and/or halo,

or R is a group of the formula -O-SO<sub>2</sub>-R<sup>b</sup>  
 wherein R<sup>b</sup> may be C<sub>1</sub>-C<sub>6</sub> alkyl or aryl optionally  
 20 substituted with C<sub>1</sub>-C<sub>6</sub> alkyl;

or R is carbamoyloxy wherein the nitrogen may  
 be substituted once or twice with C<sub>1</sub>-C<sub>6</sub> alkyl;

or R is a group of the formula -O-C(O)R<sup>c</sup>-O-  
 (C<sub>1</sub>-C<sub>6</sub> alkyl) wherein R<sup>c</sup> is a bond or C<sub>1</sub>-C<sub>6</sub> alkanediyl;

25 R<sup>1</sup> is halo, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>7</sub> alkyl  
 substituted with C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or  
 unsubstituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, or substituted or

unsubstituted C<sub>3</sub>-C<sub>7</sub> cycloalkenyl;

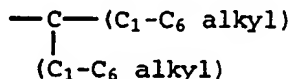
R<sup>2</sup> is O or CH<sub>2</sub>;

R<sup>3</sup> is CH<sub>2</sub> or (CH<sub>2</sub>)<sub>2</sub>;

R<sup>4</sup> is  $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}- \end{array}$ , CH<sub>2</sub>, or a bond; and

5 R<sup>5</sup> is amino, nitrilo optionally substituted  
once or twice with C<sub>1</sub>-C<sub>6</sub> alkyl; or an N-heterocyclic  
ring which optionally has another hetero atom selected  
from N, O, or S in said ring; or a pharmaceutically  
acceptable salt or solvate thereof, for use in  
10 inhibiting uterine fibrosis.

2. A compound according to Claim 1 wherein R<sup>1</sup> is  
a group having the formula



15 or a cycloalkyl group with a carbon number of three to  
eight that may be substituted with C<sub>1</sub>-C<sub>6</sub> alkyl or hydroxy.

3. A compound of Claim 2 wherein R is hydroxy.

4. A compound according to Claim 3 wherein R<sup>2</sup> is  
O and R<sup>4</sup> is CH<sub>2</sub>.

5. A compound according to Claim 1 wherein said  
25 compound is (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-  
[2-(1-pyrrolidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-  
cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-  
piperidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-  
cycloheptylbenzo[b]thien-3-yl)[4-[2-(1-  
30 pyrrolidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-  
cycloheptylbenzo[b]thien-3-yl)[4-[2-(1-

piperidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-isopropylbenzo[b]thien-3-yl)[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-isopropylbenzo[b]thien-3-yl)[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone.

6. A compound according to Claim 3 wherein R<sup>2</sup> is CH<sub>2</sub>.

7. A compound according to Claim 6 wherein said compound is (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[3-(1-pyrrolidinyl)propyl]phenyl]methanone, (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[3-(1-piperidinyl)propyl]phenyl]methanone, or (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-pyrrolidinylcarbonyl)ethyl]phenyl]methanone.

8. A compound according to Claim 2 wherein R is C<sub>1</sub>-C<sub>6</sub> alkoxy.

9. A compound according to Claim 8, wherein said compound is (6-methoxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone or (6-acetoxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone.

**SUBSTITUTE**

***REMPLACEMENT***

**SECTION is not Present**

***Cette Section est Absente***